

COVID Vaccine Requirement for Solid Organ Transplant Candidates

We deliberated as a Center, in multidisciplinary internal discussion and in consultation with colleagues at other transplant centers, for the better part of 3 months before making our decision in early December to require COVID vaccination in order to be actively listed at our Center. We reviewed published data and our own Center experience about the outcomes of solid organ transplant recipients with COVID-19 infection, the efficacy and safety records of the available vaccines, and the relative efficacy of COVID-19 vaccination both before and after solid organ transplant and the initiation of immunosuppression. We also spent an equal amount of time scrutinizing the impact such a requirement could have on our patients, particularly patients from marginalized populations or isolated areas of the state that might not have equal access to or information about the vaccine. We queried our waitlist population for the prevalence of COVID vaccination prior to our policy (85-90%) and asked patients opposed to vaccination to share with us their views. Our policy was reviewed by our health system and University leadership, Office of General Counsel, and Ethics Committee.

I think it is important to view the COVID vaccine requirement at our Center, and at other transplant centers who have such a policy, in the context of the other responsibilities and requirements we ask of all transplant patients. These include, but are not limited to, tobacco cessation, weight loss in the setting of morbid obesity, age-appropriate cancer screening, cardiac testing to screen for cardiac dysfunction and coronary artery disease, pulmonary function testing, committed caregiver support, attendance at pre-transplant education classes, substance abuse agreements stating the requirement for abstinence as a condition to listing, and CDC recommended age-appropriate vaccines. We require these things not because they necessarily have anything to do with the cause of the patient's organ failure; we require them because they help us identify and mitigate preventable causes of patient morbidity, mortality, and graft loss among immunosuppressed patients following solid organ transplant. To address your question specifically about hepatitis B vaccination series, we do require that of our transplant candidates. I realize in the current polarized public debate, COVID vaccine requirements are seen as a solitary effort by transplant centers to adjudicate around one issue. However, in fact, COVID vaccination requirements are completely in line with other transplant policies and requirements. Furthermore, the risk of severe illness and death that COVID vaccination mitigates among immunosuppressed transplant patients is far greater than the risk of events that are the subject of long existing requirements (such as the risk of major cardiac events, missed occult cancers, the impact of obesity, or tobacco-related morbidities).

Your question about previous infection, and the potential impact of natural immunity, is valid and I have appreciated the scrutiny you and others have brought to this issue. There are limited studies on the impact of previous COVID infection on the humoral and cellular immunity against SARS-CoV2 among immunosuppressed solid organ transplant recipients. There are data that suggest neutralizing antibody and cellular immunity persists past 6 months in up to 80% of patients (Transplantation 2021;105 p e52-e53; Kidney Int 2021; 99: 484-49; Kidney Int 2021; 100:238-242; total N = 95 patients). However, there are no data describing what happens to humoral and cellular immunity among unvaccinated transplant candidates with prior COVID-19

infection who then undergo solid organ transplant, with associated induction immunosuppression. One might reasonably assume it is less than the 80% protection reported in the studies above, which largely included stable transplant recipients who were years post-transplant. One other practical challenge, as you are aware, is that we cannot predict with any certainty the amount of immunosuppression that a given recipient might require, and the impact of events such as acute rejection that can necessitate a sudden and substantial increase in immunosuppression. I do hope that we learn more about the impact of prior infection in the end-organ failure population, and develop assays that provide a better sense of functional immunity rather than quantitative estimates of humoral and cellular responses.

Before giving my personal opinion on this issue, I would clarify a few additional points that we believe provide sound medical justification for our COVID vaccine policy. First, the risk of severe illness and death among unvaccinated solid organ transplant recipients is real and horrific. Initial reports from Wuhan, Europe, and New York reported death rates among solid organ transplant recipients as high as 30-50%. Even in the era of better antiviral therapies, improved critical care strategies, and monoclonal antibodies (which we have been using aggressively in transplant recipients), the death rate is still somewhere between 3 and 10% in published studies. In addition, the morbidity of COVID infection in these patients in terms of graft injury, secondary infection, chronic lung injury, and debilitation is substantial and intolerable.

Second, vaccination prior to transplant is clearly superior to vaccination after transplant and initiation of immunosuppression. Even with a “control” group of chronically ill end organ failure patients like the dialysis population, humoral and cellular responses appear much more robust and durable than in the post-transplant population.

Third, we believe the vaccines are exceedingly safe, particularly when compared to the many other interventions and medications that patients will require after transplant.

Finally, we offer exceptions to the vaccine requirement to patients who present to us critically ill in need of immediate transplant such that time to complete a vaccine series is not possible. Examples include patients with acute liver failure or severe cardiogenic shock in immediate need of transplant. We view these patients differently, as they did not have the time to consider the vaccine requirement or other usual pre-transplant required activities (for example, we don't require such patients to attend required education classes or document tobacco cessation). These fulminant organ failure patients are rare, constituting less than 3-4% of patients transplanted nationally in the US.

In closing, I want to offer my personal thoughts about this topic. These are my own opinions but I think represent that of the vast majority of the transplant community and are in line with recommendations published by most of the major transplant societies.

We are humbled to work in what I believe is the most transformative field in medicine. We are committed to helping patients with end-organ failure regain their health and quality of life, when they have no other options. This is a solemn responsibility to which we commit our

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careers and much of our lives. But we carry one even greater responsibility, and that is to be the steward of the most precious resource in medicine – an organ donated by a living or deceased individual to save the live of another person. Without organ donation, none of this exists.

Furthermore, we have a profound mismatch in the supply of donor organs relative to supply. The consequences of that disparity are not annoying or inconvenient, they are deadly. To give a specific example, in recent years we have performed 8500-9000 liver transplants annually in the US. Each year, nearly 2000 people die on the waiting list or are removed because they have become too ill for transplant. Thus, for every 4-5 patients we transplant, one person dies who didn't get their chance. In that context, any preventable post-transplant death or graft loss is unacceptable. It is unacceptable to the patients on the list who could have potentially had that chance at transplant, and it is unacceptable use of the gift provided by the organ donor. I suspect if we in fact had the shortage of ventilators we feared in early 2020, and for every 4-5 patients we placed on ventilator, one person died without one, we would think much differently about who we placed on ventilators. These are not theoretical arguments or political debates, these are real lives that we witness saved and lost in our work every day. It is our duty to provide transplant patients the best possible outcome – for themselves first and foremost, for the other individuals who are still waiting and haven't had their chance, and most of all to be good stewards for the gift of organ donation.

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